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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/604,779	08/15/2003	Matt Ewert	USF-196TCXC1	1778

23557 7590 04/19/2007

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EXAMINER	
PETERSEN, CLARK D	
ART UNIT	PAPER NUMBER
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/604,779	EWERT ET AL.	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2,7-47,49 and 50* is/are rejected.

7)☐ Claim(s) *3-6 and 48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 29 January 2007, in which claims 1, 3, 4, 6-10, 13, 16-19, 23, 27, 31, 32, 34-39, and 41 were amended, and new claims 44-50 were presented.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All objections and rejections not repeated in the instant Action have been withdrawn due to Applicant's response to the previous Action.

Specification

Applicants' amendment to the specification, specifically at paragraphs [0065] and [0026], is acknowledged.

Claim Objections

In the Office Action mailed 24 July 2006, claims 16 and 17 were objected to. Based on Applicants' amendment, that objection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16 and 18-30 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

This is a new rejection necessitated by Applicants' amendment.

Evidence that claims fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the reply filed 29 January 2007. In that paper, Applicants have amended claim 16 to overcome the rejection under 35 USC 112, second paragraph, as being vague and indefinite. However, as amended, the claims do not encompass Applicants' invention. Applicants amended claim 16 to recite "the buffer solution". "The buffer solution" is characterized as "containing plasminogen and streptokinase". Subsequent dependent claims 18 and 23 recite that "the buffer solution" is centrifuged. However this would not seem logical; it seems Applicants intend to centrifuge the mixture resulting from the addition of "the buffer solution to the volume of blood" (claim 16). Due to antecedent basis, as currently written, the claims recite that the buffer solution is centrifuged before addition to any blood, and analysis is carried out in the absence of any blood sample; based on logic and support in the specification (see paras [0054] to [0060], for example) this would not seem to accurately claim Applicants' intention. Please amend the claims or revise antecedent basis such that Applicants' invention is accurately claimed.

Claims 16-43 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This is a new rejection.

Claim 16 recites "the volume of blood". Although appearing to refer to the whole blood sample of claim 1, the phrase lacks antecedent basis.

Claims 17-43 and 50 are rejected because they depend from claim 16.

Claims 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This is a new rejection.

Claims 23-30 recite "the sample". There is no antecedent basis for "the sample", other than in claim 1. However using "the whole blood sample" as the antecedent for "the sample" in claim 1 leaves claim 23, for example, indefinite, because claim 23 recites the division of the sample of claim 1 into two parts.

Claims 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This is a new rejection.

Claims 33 and 34 recite "the buffer". It appears Applicants are referring to the previously cited "buffer solution", however there is no antecedent basis for "the buffer".

Claims 39-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This is a new rejection.

Claims 39-43 refer to the "trehalose storage buffer". It appears Applicants are referring to the previously cited "trehalose buffer", however there is no antecedent basis for "the trehalose storage buffer".

Response to arguments - 35 USC § 112

In the Office Action mailed 24 July 2006, claims 16-43 were rejected under 35 USC 112, second paragraph, as indefinite because they lacked antecedent basis for "the dried reagents", "the solution", and "the dried reagent" (singular). Based on Applicants' amendment, that rejection is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7, 8, 44, and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang, et al (J Clin Microbiol, 1995).

This rejection was presented in the Office Action mailed 24 July 2006, and is slightly modified as necessitated by Applicants' amendment.

Zhang et al teach a method of collecting blood from patients. This blood is collected into tubes containing acid citrate, a coagulant, therefore reading on claims 44 and 45 (see "Inoculation of whole blood with *S. pneumoniae*", p. 597, col. 1, for example). The blood is then broken up with buffer ATL which comprises SDS and Proteinase K. The purified DNA is then subjected to PCR amplification, successfully showing the presence of *Streptococcus pneumoniae* DNA in patients' blood (see Materials and Methods, p. 597, see Results, p. 599; see Table 3, p. 600, as examples). Therefore the teachings of Zhang et al are deemed to anticipate the instant claims 1, 7, 8, 44, and 45.

Claims 1, 7-10, 44, 45, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (1995) in light of Nadano et al (Clin Chem, 1993) and Snitko et al (Biochem J, 1997).

This is a new rejection necessitated by Applicants' amendment.

The teachings of Zhang et al are discussed above.

Nadano et al teach that active DNase is present in leukocytes and erythrocytes as well as serum (see Tables 1 and 2, p. 451, for example). Therefore any blood sample must be inherently exposed to DNase, which is an endonuclease.

Snitko et al teach that phospholipase A2 is secreted from blood cells in response to inflammatory stimuli, of which bacterial infection is one (see Introduction, p. 737, for

example). Therefore, the teachings of Zhang et al in light of Snitko et al are deemed to anticipate the instant claims 1, 7-10, 44, 45, and 47.

Claims 1, 2, 7, 9, 10, and 44-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Watson (J Clin Microbiol, 1978).

This is a new rejection.

Watson et al teach a method of trapping bacteria from blood samples in a clot, then digesting the clot by adding streptokinase, and culturing the bacteria for identification. Watson et al remove 4-8 ml blood samples from patients suspected of having enteric fever. They add this blood to a medium containing sodium taurocholate which is a bile salt surfactant, reading on a detergent, and which also contains 100 U streptokinase. The addition of taurocholate and streptokinase dissolves the clot, and allows the organisms to be cultured for identification and counting (see p. 123, col. 2, to p. 124, col. 1). The method used by Watson is congruent with the procedure described in the specification (see paras [0045] and [0046]). In particular, in one experiment, they add the entire volume of serum with the clot (see "Effect of fresh and heated immune serum on *S. typhi*", p. 124, col. 1, for example). Regarding the limitation that the sample is exposed to plasminogen, the whole blood sample must be inherently exposed to plasminogen because blood is known to contain plasminogen, and streptokinase would not dissolve clots without activating downstream plasminogen.

Therefore the teachings of Watson are deemed to anticipate the instant claims 1, 2, 7, 9, 10, and 44-46.

Claims 1, 7, 9, 10, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Zierdt et al (J Clin Microbiol, 1977) in light of Mansour et al (US 4,693,972, issued 15 Sep 1987).

This is a new rejection.

Zierdt et al teach a method of purifying bacteria from blood. They add Triton X-100 (octylphenol ethoxylate) as well as an enzyme mixture called Rhozyme 41 to blood cultures, resulting in dissolution of blood components. The lysed solution is then passed through a vacuum filter, collecting intact bacteria. These bacteria are then cultured for identification. The pH of the solution in which the lysis is carried out is 7.8 (see Materials and Methods, pp. 46-48, for example).

Therefore the teachings of Zierdt et al are deemed to anticipate the instant claims 1, 7, 9, 10, and 50.

Response to arguments - 35 USC § 102

Applicants traverse the rejection of claims 1, 7, and 8 under 35 USC 102(b) as being anticipated by Zhang et al (1995). Applicants assert that Zhang teaches pre-treatment of blood by vortexing the blood with glass beads prior to addition of enzyme/detergent combination. However in claims 1, 7, and 8, and by extension new claims 44, and 45, Applicants claim a method *comprising* treatment of whole blood with an enzyme/detergent combination, which therefore does not rule out other steps including vortexing of the sample.

Applicants traverse the rejection of claims 1 and 2 under 35 USC 102(b) as being anticipated by Cassels et al (Biochem J, 1987). Based on Applicants' amendment of claim 1 to recite "whole blood", this rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 7, 9, 10-12, 16, 18, 19, 31 and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Dupe et al (Thrombos Haemostas, 1981).

This is a new rejection necessitated by Applicants' amendment.

The teachings of Watson et al are discussed above and applied as before.

Watson et al do not expressly teach maintaining plasminogen and streptokinase in a frozen state, or that the solution should comprise NaCl, or that the streptokinase/plasminogen should be kept in a dried state, or that the plasminogen and streptokinase are mixed and distributed in disposable test containers, or that the plasminogen and streptokinase are resuspended in a buffer solution and added to blood and incubated at room temperature, or that the mixture should be centrifuged, the supernatant decanted, and the pellet washed.

Dupe et al teach a method of assaying thrombus dissolution by streptokinase/plasminogen complexes in whole blood; for example they measure the *in vivo* dissolution of a blood clot in a rabbit (see Results, "Establishment of the Animal Model", p. 530-1, for example). They teach that streptokinase and plasminogen can be prepared ahead of time. They also teach that at the time their study was written, plasminogen and streptokinase were both available in a pharmaceutical grade lyophilized powder. The companies that provide them mix them and ship them in disposable containers; for example see "Type 3 complex", SK-human plasmin activator complexes. They also teach that the streptokinase/plasminogen mix is active at room temperature (for teaching of all claim limitations see "Fibrinolytic agents", p. 530, for example). Regarding the limitations recited in claims 18 and 19, practice of separating clots from serum by centrifugation has been well established in the art of clinical hematology for decades.

A person of ordinary skill in the art at the time the invention was made would have been motivated to prepare streptokinase and plasminogen in either a frozen or lyophilized form because Dupe et al teach that they can be stored for longer periods of time preserved in such a manner, and Watson et al teach that streptokinase is a useful reagent for isolating bacteria from blood cultures.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to freeze or lyophilize streptokinase and plasminogen to store for later use in a method of isolating bacteria.

Claims 1, 2, 7, 9, 10-12, 16, 18-22, 31 and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Dupe et al (Thrombos Haemostas, 1981) and further in view of Semple et al (Bioorg and Medicin Chem Lett, 2000).

This is a new rejection.

The teachings of Watson and Dupe et al are discussed above and applied as before.

Semple et al teach that the protease inhibitor ecotin (also referred to as ecotine) is a powerful anticoagulant produced by some varieties of *E. coli*; it inhibits portions of the protease cascade that leads to fibrin clot formation (see Abstract; see Introduction; see Inhibitor Design Strategy, p. 2305). Further, they suggest that ecotin's activity could be useful in various applications in preventing thrombosis, i.e. clot formation (see, Abstract, p. 2305, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use sucrose and ecotine washes of pellets when performing the assay of liberating particles from blood taught by Watson, because Watson teaches that one can trap bacteria in blood clots, followed by dissolving the clots to liberate the bacteria, and Sempel et al teach that it is a powerful anticoagulant and would prevent accretion of undesirable coagulated blood proteins in the desired pellet. Additionally, one of ordinary skill in the art knows that sucrose and HEPES can be useful as washing agents because they are well-established biological buffers. One would have been

motivated to do so for the expected benefit that using ecotine and sucrose in a HEPES buffer would yield a better-purified pellet.

Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, one would have a reasonable expectation of success in practicing the claimed invention.

Claims 1, 2, 7, 9, 10-13, 16, 18, 19, 27, 31, 44-46 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Dupe et al (Thrombos Haemostas, 1981) and further in view of Zierdt (J Clin Microbiol, 1982) in light of Mansour et al (US 4,693,972, issued 15 Sep 1987).

This is a new rejection.

The teachings of the three cited references are discussed above and applied as before.

Additionally, Mansour et al teach that Zierdt's reagent, i.e. Rhozyme 41, comprises a protease, a lipase and a nuclease. Furthermore, as discussed above, Zierdt teaches that the solution, once lysed, should be passed through a filter, which collects intact bacteria. These bacteria can be detected by impedance detection, reading on claim 31 (see p. 47, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to add endonuclease and lipase in a method of isolating bacteria from a blood sample because Zierdt teaches that addition of Rhozyme 41 is a gentle method of dissolving components of blood while leaving bacteria intact, and Watson

teaches that bacteria can then be separated from blood by inducing a clot which captures bacteria and then is dissolved by streptokinase.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to isolate bacteria with a method involving addition of lipase, endonuclease, and streptokinase to blood.

Claims 1, 2, 7, 9, 10-12, and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (J Clin Microbiol, 1978) in view of Smith et al (Thromb Haemostas, 1982).

The teachings of Watson are discussed above and applied as before.

Watson et al do not expressly teach that enzymes are freeze dried for storage.

Smith et al teach that plasminogen and streptokinase can be separately purified and lyophilized in individual containers for long-term storage (see "Fibrinolytic agents", p. 269, col. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to lyophilize plasminogen and streptokinase because Smith et al teach that these enzymes retain activity when preserved in this manner, and preservation allows for long-term storage of useful reagents.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to lyophilize streptokinase and plasminogen in preparation for isolating bacteria from blood in the method of Watson.

Claims 1, 2, 7, 9, 10, and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (J Clin Microbiol, 1978) in view of Cassels et al (Thromb Haemostas, 1982).

This is a new rejection.

The teachings of Watson are discussed above and applied as before.

Watson does not expressly teach the use of phosphate in a storage solution.

Cassells et al teach that phosphate is a suitable medium for carrying out reactions comprising plasminogen and streptokinase (see "Clot-lysis assay, p. 396, col. 2, for example). Additionally it is standard practice in the art of protein purification to snap-freeze proteins in phosphate-buffered saline, for example for storage.

A person of ordinary skill in the art at the time the invention was made would have been motivated to freeze streptokinase in a phosphate buffer because Cassels et al teach that a phosphate buffer is compatible with streptokinase activity, and it is well-known in the art to freeze proteins in a phosphate buffer such as PBS, for example.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to freeze streptokinase in a phosphate buffer.

Claims 1, 7, 9, 10-16, 18, 19, 31 and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Dupe et al (Thrombos Haemostas, 1981) and further in view of Kreilgaard et al (1998).

This is a new rejection necessitated by Applicants' amendment.

The teachings of Watson et al and Dupe et al are discussed above and applied as before.

Neither Watson nor Dupe expressly teaches the lyophilization of streptokinase or plasminogen in trehalose.

Kreilgaard et al teach that proteins have poor stability in aqueous solution. They further state that this problem can be overcome by freeze-drying proteins; however in this process, proteins often aggregate and lose their enzymatic activity. Therefore, trehalose can be added to a protein before the freeze drying process and that trehalose affords protection to enzymes during freeze drying and storage as a dried solid (see, Introduction, p. 121, col. 2, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include trehalose in a method of freeze drying an enzymatic combination taught by Dupe et al because Dupe et al teach that it is possible to freeze dry enzymes in separate vials that are to be used later in a process of liberating particles from blood, and Kreilgaard et al teach that trehalose is a useful sugar to add to a enzyme composition before freeze-drying. One would have been motivated to do so for the expected benefit the enzyme composition for liberating particles from blood would be better protected and therefore more active.

Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, one would have a reasonable expectation of success in practicing the claimed invention.

Claims 1, 2, 7-11, 16, 18, 19, 23-31, 33, 34, 44-46, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Zhang et al (1995) in view of Dupe et al (1981), in view of Zierdt et al (1977) and in view of Hallick et al (Nucleic Acid Res, 1977).

The teachings of Watson (1978), Zhang et al (1995) and Dupe et al (1981) are discussed above and applied as before.

Additionally, Zhang et al teach that blood samples can be lysed using glass beads and vortexing, and then centrifuged to remove gross blood byproducts before the supernatant is decanted and processing continued with a Qiagen blood mini amp kit (see Materials and Methods, p. 597, for example). The Qiagen blood mini amp kit teaches the use of proteinase K and SDS as components of the process of purifying DNA from blood samples (see Qiagen DNA blood mini kit handbook, p. 12, for example). Also as discussed above, Zhang et al teach the use of citrate as an anticoagulant.

None of the above references expressly teaches the use of endonuclease inactivation, DNAse inactivation, or addition of aurintricarboxylic acid to the sample.

None of the references teaches the inclusion of octylphenol ethoxylate (Triton X-100).

Hallick et al teach that aurintricarboxylic acid (ATA) is a general nuclease inhibitor (see Introduction, p. 3055, for example). They demonstrate that addition of ATA to a nuclease reaction inhibits the reaction (see Figs 1 and 2, p. 3058, for example). Additionally they suggest that it would be useful to add ATA to prevent

degradation of nucleic acids during nucleic acid isolation (see Introduction, p. 3055, for example).

Zierdt et al (1977) teach that Triton X-100 is advantageously added to a blood solution in a method of purifying bacteria present in the blood. The procedure allows one to lyse blood cells without damaging the bacteria (see Materials and Methods, p. 46, col. 2, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add ATA and Triton X-100 when performing the assay of liberating particles, because Zhang et al teach that one can perform PCR from purified bacterial DNA, Zierdt et al teach that one can isolate bacteria from whole blood in a method comprising Triton X-100, and Hallick et al teach that addition of ATA inhibits nucleases and suggest its usefulness when one desires to purify DNA. One would have been motivated to do so for the expected benefit that using ATA and Triton X-100 would provide higher yields of quality DNA.

Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, one would have a reasonable expectation of success in practicing the claimed invention.

Claims 1, 2, 7-11, 16, 18, 19, 23-31, 33, 34, 39, 44-46, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Zhang et al (1995) in view of Dupe et al (1981) in view of Hallick et al (Nucleic Acid Res, 1977) and in view of Zierdt (J Clin Microbiol, 1982).

This is a new rejection.

The teachings of Watson (1978), Zhang et al (1995) Dupe et al (1981) and Hallick et al (1977) are discussed above and applied as before.

None of the references expressly teaches the use of 10 mM potassium phosphate.

Zierdt teaches that the buffer should contain 10 mM sodium phosphate (see p. 172, col. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to use potassium phosphate in a method of isolating bacteria because Zierdt teaches that a 10 mM sodium phosphate buffer is suitable in a method of isolating bacteria from blood, and potassium phosphate is a suitable equivalent.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a 10 mM potassium phosphate buffer in a method of isolating bacteria from blood.

Response to arguments - 35 USC § 103

Applicants traverse the rejection of claims 1-43 under 35 USC 103(a). Based on Applicants' amendments and arguments, the previous rejections under 35 USC 103(a) have been withdrawn.

However Examiner continues to rely on individual references to build an argument for rejection of claims under 35 USC 103(a), so Applicants' arguments

regarding various citations are addressed below. In particular, the Cassels reference, the Smith reference, and the Hallick reference continue to be relied upon.

Regarding the Smith and Cassels reference, Examiner admits the references do not teach that streptokinase and plasminogen should be frozen *before* the reaction occurs. Dupe et al for example concur with Applicants, in that frozen pre-activated complexes do not exhibit thrombolytic activity *in vivo* in rabbits (reading on whole blood; see pp. 532-533). However the lyophilization of streptokinase and plasminogen is widely cited in the art. Both are available from commercial vendors, and are expressly described by the cited references.

Regarding the Hallick reference, Applicants argue that the subject invention teaches away from the teachings of Hallick. However the use of ATA as currently claimed requires that the user add the ATA at the step of digestion, after the step of blood lysis (see Claims 26 and 30). This is consistent with Hallick's recommendation that addition of ATA is useful in preserving the nucleic acids for analysis, after the step of digesting the crude sample. Therefore Examiner maintains the assertion that the use of ATA as instantly claimed is not novel.

Claim Objections

Claims 3-6 and 48 are objected to as depending from rejected claims.

Conclusion

Claims 3-6, 17, 26, 36, 37, 38, and 48 are free of the art.

Examiner has provided new grounds for rejection in this Action. Therefore, this Action is NOT FINAL.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP
4/12/2007

Jon Weber
Supervisory Patent Examiner